PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	03.08.2004
Applicant's or agent's file reference 32/43/64087WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/01404	31.03.2003	02.04.2002

Applicant
NORBROOK LABORATORIES LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
32/43/64087WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/01404	31.03.2003	02.04.2002
International Patent Classification (IPC) or both national classification and IPC		
A61K47/10		
Applicant		
NORBROOK LABORATORIES LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
31.10.2003	03.08.2004

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/01404

I. Basis of the report

1. With regard to the elements of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-10 as originally filed

Claims, Numbers

1-16 filed with telefax on 16.06.2004

Drawings, Sheets

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

see separate sheet

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☐ claims Nos.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 10 are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-16
Industrial applicability (IA)	Yes:	Claims	1-16
	No:	Claims	

2. Citations and explanations

see separate sheet

SECTION I. .....

item 5.
With letter dated 16.06.04, the applicant filed a set of claims which comprises subject-matter which is considered to go beyond the disclosure as filed. The feature in question relates to the lower limit of 2,4% of the range according to which the poloxamer is to be applied according to independent claims 1 and 12.

The applicant referred with respect to original disclosure of the said technical feature in particular to Example 3 of present description which shows the use of a poloxamer in an amount of 2,4%. Although the originally claimed percentage range of 0,5 - 20% (w/v) of the poloxamer comprises the now specified one, however, the value has been taken out of a composition comprising further components and no clear indication is available that a generalisation as now made in the independent claims is justified.

SECTION III. .....

item 1.
The specific embodiment of claim 10 specifies the lower limit of the Carprofen as being lower than that of the independent claim 1 to which it refers. Thus the requirements of clarity according to Article 6 PCT are not fulfilled.

SECTION V. .....

For the present evaluation of the requirements of Article 33 PCT (see SECTION I., item 5), the percentage range of the poloxamer to be applied in the injectable solution is that specified in the originally filed independent claim 1, *ie* 0,5 - 20% (w/v).

1. Reference is made to the following documents:

   D1: EP-A-0 955 063
   D2: CH-A-663 788
   D3: US-A-5 283 067

2. The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matters of the independent product claims 1, 12, 15 and 16

do not involve an inventive step (Rule 65(1)(2) PCT).

The claimed product, ie the aqueous injectable solution comprises in certain amounts

- Carprofen (6-chloro-α-methyl-carbazole-2-acetic acid)

and

- a poloxamer.

Such a solution differs from solutions disclosed in D1 (see *eg* claim 1; paragraphs [0021] and [0024]) only by the fact that the compound Carprofen has not explicitly been mentioned. However, D1 clearly stated that anti-inflammatory compounds can advantageously be used in combination with poloxamers to arrive at injectable solutions solving to same problem, *ie* to provide anti-inflammatory drugs suitable for injection. Carprofen is well known to the person skilled in the art as being such a compound and its substitution in the solutions according to D1 must be considered obvious, this the more, as *eg* D2 (see *eg* claim 6) suggests its usability for anti-inflammatory purposes. The person skilled in the art gets furthermore the information from D3 (see *eg* claim 1; Example 4) that injectable aqueous solutions comprising poloxamers and anti-inflammatory agents can successfully be prepared to solve the said problem.

The reasoning is valid mutatis mutandis for independent method claim 12 and for the embodiments claimed in claims 15 and 16 referring to Examples described in the description.

The claimed subject-matter lacks therefore an inventive step.

It is noted that the Comparative Examples as presented in the description on page 8, fall under the wording of present independent product claims, thus any surprising effect derived by the specified injectable solution cannot be seen.

Essentially, the dependent claims specify certain Carprofen salts which are known from D2, or define the poloxamer which can be taken from *eg* D1, and indicate that further components can be present. To arrive at these embodiments the person skilled in the art can take corresponding information from D1, thus any inventive step must also be denied for the dependent claims.

The applicant provided during the international preliminary examination procedure

arguments with respect to certain disclosure of documents D1 - D3, however, as there is also disclosure available as specified above, a different view with respect to the requirements of the PCT cannot be given.

3. Claims 15 and 16 comprise references to the description, ie to Examples. According to Rule 6.2(a) PCT, claims should not contain such references except where absolutely necessary, which is not the case here.

CLAIMS

1. A room-temperature stable injectable solution for veterinary use comprising from 0.5 to 30% (w/v) of Carprofen (6-chloro-α-methyl-carbazole-2-acetic acid) or a physiologically acceptable salt of Carprofen, and from 2.4% to 12% (w/v) of a poloxamer, and water *q.s.* for injection.

2. An injectable aqueous solution according to Claim 1, wherein the Carprofen salt is in the form of an arginine salt.

3. An injectable aqueous solution according to Claim 1, wherein the carprofen salt is in the form of a lysine salt.

4. An injectable aqueous solution according to any one of Claims 1 to 3, wherein Carprofen is present in an amount of from 2.5 to 7.5% (w/v).

5. An injectable aqueous solution according to any one of Claims 1 to 3, wherein Carprofen is present in an amount of from 2.5 to 5% (w/v).

6. An injectable aqueous solution according to any one of Claims 1-5, comprising arginine in an amount of from 1 to 20% (w/v).

7. An injectable aqueous solution according to Claim 1, wherein an organic solvent is present with the poloxamer.

8. An injectable aqueous solution according to Claim 7, wherein the organic solvent is present in the range of 0.5 to 20% (w/v).

9. An injectable aqueous solution according to Claim 1, wherein the poloxamer is $HO(CH_2CH_2O)_x(CCH_3HCH_2O)_y(CH_2CH_2)_zH$ wherein x is 75, y is 30 and z is 75.

10. An injectable aqueous solution for veterinary use according to Claim 1, where the solution is to be employed in treating felines, wherein the lower limit of the range of Carprofen is 0.25% (w/v).

11. An injectable aqueous solution for veterinary use according to Claim 10, comprising arginine in an amount of from 1 to 20% (w/v).

12. A method of producing a room-temperature stable injectable aqueous solution for veterinary use comprising bringing together Carprofen or a physiologically acceptable salt thereof, a poloxamer, and adding sufficient water for injection, to provide a solution containing from 0.5 to 30% (w/v) of Carprofen (6-chloro-α-methyl-carbazole-2-acetic acid) or a physiologically acceptable salt of Carprofen, and from 2.4% to 12% (w/v) of poloxamer.

13. A method according to Claim 12, wherein the poloxamer is $HO(CH_2CH_2O)_x(CCH_3HCH_2O)_y(CH_2CH_2)_zH$ wherein x is 75, y is 30 and z is 75.

14. A method of producing an injectable aqueous solution according to Claim 12 or Claim 13, wherein said method further comprises the inclusion of a preservative.

15. An injectable aqueous solution for veterinary use according to any one of the Examples 1 to 19 hereinbefore.

16. A method of producing an injectable aqueous solution substantially as described in the Example 1.